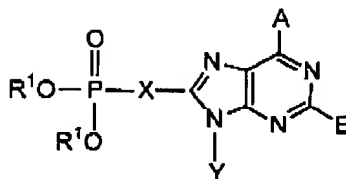


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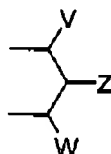
wherein

A is selected from the group consisting of $-\text{NR}^8$, $-\text{NHSO}_2\text{R}^3$, $-\text{OR}^5$, $-\text{SR}^5$, halo, lower alkyl, $-\text{CON}(\text{R}^4)_2$, guanidino, amidino, $-\text{H}$, and perhaloalkyl;

E is selected from the group consisting of $-\text{H}$, halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, $-\text{CN}$, and $-\text{NR}^7$;

X together with Y forms a cyclic group selected from the group of heterocyclic, and aryl;

R^1 is independently selected from the group consisting of $-\text{H}$, alkyl, aryl, heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-\text{C}(\text{R}^2)_2\text{-aryl}$, $-\text{alk-aryl}$, $-\text{C}(\text{R}^2)_2\text{OC}(\text{O})\text{NR}^2$, $-\text{NR}^2\text{-C}(\text{O})\text{-R}^3$, $-\text{C}(\text{R}^2)_2\text{-OC}(\text{O})\text{R}^3$, $-\text{C}(\text{R}^2)_2\text{-O-C}(\text{O})\text{OR}^3$, $-\text{C}(\text{R}^2)_2\text{OC}(\text{O})\text{SR}^3$, $-\text{alk-S-C}(\text{O})\text{R}^3$, $-\text{alk-S-S-alkylhydroxy}$, and $-\text{alk-S-S-S-alkylhydroxy}$, or together R^1 and R^1 are $-\text{alk-S-S-alk-}$ to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together R^1 and R^1 are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-\text{R}^9$; or

together V and Z are connected via a chain of 3-5 atoms, only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy, alkoxy, or aryloxy, attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy, alkoxy, alkylthiocarboxy, hydroxymethyl, or aryloxy, attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

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C1
Z is selected from the group consisting of $-\text{CH}_2\text{OH}$, $-\text{CH}_2\text{OCOR}^3$, $-\text{CH}_2\text{OC(O)SR}^3$, $-\text{CH}_2\text{OCO}_2\text{R}^3$, $-\text{SR}^3$, $-\text{S(O)R}^3$, $-\text{CH}_2\text{N}_3$, $-\text{CH}_2\text{NR}^2_2$, $-\text{CH}_2\text{Ar}$, $-\text{CH(Ar)OH}$, $-\text{CH}(\text{CH}=\text{CR}^2\text{R}^2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^2)\text{OH}$, and $-\text{R}^2$;

with the provisos that:

- a) V, Z, W are not all -H; and
b) when Z is $-\text{R}^2$, then at least one of V and W is not -H or $-\text{R}^2$;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

R^4 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

R^6 is independently selected from the group consisting of -H, and lower alkyl;

R^7 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and $-\text{C(O)R}^{10}$;

R^8 is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-\text{C(O)R}^{10}$, or together said R^8 groups form a bidendate alkylene;

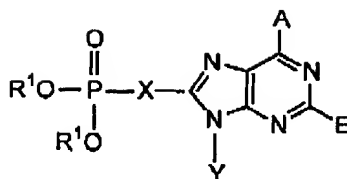
R^9 is selected from the group consisting of alkyl, aralkyl, , heteroalicyclic, and alicyclic;

R^{10} is selected from the group consisting of -H, lower alkyl, $-\text{NH}_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, $-\text{OH}$, $-\text{NH}_2$ and $-\text{OR}^3$; and pharmaceutically acceptable prodrugs and salts thereof.

C2
34. (Twice Amended) A method of treating an animal for diabetes mellitus, comprising administering to said animal a therapeutically effective amount of a compound of formula (1):

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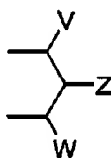
wherein

A is selected from the group consisting of $-NR^8$, $-NHSO_2R^3$, $-OR^5$, $-SR^5$, halo, lower alkyl, $-CON(R^4)_2$, guanidino, amidino, $-H$, and perhaloalkyl;

E is selected from the group consisting of $-H$, halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, $-CN$, and $-NR^7$;

X together with Y forms a cyclic group selected from the group of heterocyclic, and aryl;

R^1 is independently selected from the group consisting of $-H$, alkyl, aryl, heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)_2$ -aryl, $-alk-aryl$, $-C(R^2)_2OC(O)NR^2$, $-NR^2-C(O)-R^3$, $-C(R^2)_2-OC(O)R^3$, $-C(R^2)_2-O-C(O)OR^3$, $-C(R^2)_2OC(O)SR^3$, $-alk-S-C(O)R^3$, $-alk-S-S-alkylhydroxy$, and $-alk-S-S-S-alkylhydroxy$, or together R^1 and R^1 are $-alk-S-S-alk-$ to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together R^1 and R^1 are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^6$; or

together V and Z are connected via a chain of 3-5 atoms, only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

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C2
Z is selected from the group consisting of $-\text{CH}_2\text{OH}$, $-\text{CH}_2\text{OCOR}^3$, $-\text{CH}_2\text{OC(O)SR}^3$, $-\text{CH}_2\text{OCO}_2\text{R}^3$, $-\text{SR}^3$, $-\text{S(O)R}^3$, $-\text{CH}_2\text{N}_3$, $-\text{CH}_2\text{NR}^2$, $-\text{CH}_2\text{Ar}$, $-\text{CH(Ar)OH}$, $-\text{CH(CH=CR}^2\text{R}^2)\text{OH}$, $-\text{CH(C=CR}^2\text{R}^2)\text{OH}$, and $-\text{R}^2$;

with the provisos that:

- a) V, Z, W are not all -H; and
b) when Z is $-\text{R}^2$, then at least one of V and W is not -H or $-\text{R}^9$;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

R^4 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

R^6 is independently selected from the group consisting of -H, and lower alkyl;

R^7 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and $-\text{C(O)R}^{10}$;

R^8 is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-\text{C(O)R}^{10}$, or together said R^8 groups form a bidendate alkylene;

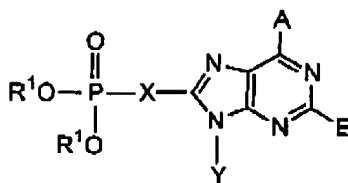
R^9 is selected from the group consisting of alkyl, aralkyl, , heteroalicyclic, and alicyclic;

R^{10} is selected from the group consisting of -H, lower alkyl, $-\text{NH}_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, $-\text{OH}$, $-\text{NH}_2$ and $-\text{OR}^3$; and pharmaceutically acceptable prodrugs and salts thereof.

35. (Twice Amended) A method of lowering blood glucose levels in an animal in need thereof, comprising administering to said animal a pharmaceutically acceptable amount of a compound of formula (1):

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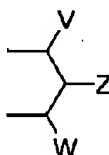
wherein

A is selected from the group consisting of $-NR^8$, $-NHSO_2R^3$, $-OR^5$, $-SR^5$, halo, lower alkyl, $-CON(R^4)_2$, guanidino, amidino, $-H$, and perhaloalkyl;

E is selected from the group consisting of $-H$, halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, $-CN$, and $-NR^7$;

X together with Y forms a cyclic group selected from the group of heterocyclic, and aryl;

R^1 is independently selected from the group consisting of $-H$, alkyl, aryl, heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)_2$ -aryl, $-alk-aryl$, $-C(R^2)_2OC(O)NR^2$, $-NR^2-C(O)-R^3$, $-C(R^2)_2-OC(O)R^3$, $-C(R^2)_2-O-C(O)OR^3$, $-C(R^2)_2OC(O)SR^3$, $-alk-S-C(O)R^3$, $-alk-S-S-alkylhydroxy$, and $-alk-S-S-S-alkylhydroxy$, or together R^1 and R^1 are $-alk-S-S-alk-$ to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together R^1 and R^1 are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected via a chain of 3-5 atoms, only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

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Z is selected from the group consisting of $-\text{CH}_2\text{OH}$, $-\text{CH}_2\text{OCOR}^3$, $-\text{CH}_2\text{OC(O)SR}^3$, $-\text{CH}_2\text{OCO}_2\text{R}^3$, $-\text{SR}^3$, $-\text{S(O)R}^3$, $-\text{CH}_2\text{N}_3$, $-\text{CH}_2\text{NR}^2_2$, $-\text{CH}_2\text{Ar}$, $-\text{CH(Ar)OH}$, $-\text{CH}(\text{CH}=\text{CR}^2\text{R}^2)\text{OH}$, $-\text{CH}(\text{C}=\text{CR}^2)\text{OH}$, and $-\text{R}^2$;

with the provisos that:

- a) V, Z, W are not all $-\text{H}$; and
b) when Z is $-\text{R}^2$, then at least one of V and W is not $-\text{H}$ or $-\text{R}^9$;

R^2 is selected from the group consisting of R^3 and $-\text{H}$;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

R^4 is independently selected from the group consisting of $-\text{H}$, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

R^6 is independently selected from the group consisting of $-\text{H}$, and lower alkyl;

R^7 is independently selected from the group consisting of $-\text{H}$, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and $-\text{C(O)R}^{10}$;

R^8 is independently selected from the group consisting of $-\text{H}$, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-\text{C(O)R}^{10}$, or together said R^8 groups form a bidendate alkylene;

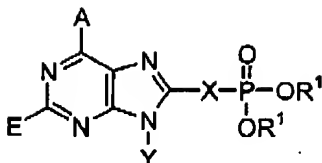
R^9 is selected from the group consisting of alkyl, aralkyl, , heteroalicyclic, and alicyclic;

R^{10} is selected from the group consisting of $-\text{H}$, lower alkyl, $-\text{NH}_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, $-\text{OH}$, $-\text{NH}_2$ and $-\text{OR}^3$; and pharmaceutically acceptable prodrugs and salts thereof.

36. (Twice Amended) A method of inhibiting FBPase at the AMP site in patients in need thereof, comprising administering to said patients an FBPase inhibitory amount of a compound of formula (1):

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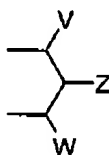
wherein

A is selected from the group consisting of $-\text{NR}^8$, $-\text{NHSO}_2\text{R}^3$, $-\text{OR}^5$, $-\text{SR}^5$, halo, lower alkyl, $-\text{CON}(\text{R}^4)_2$, guanidino, amidino, $-\text{H}$, and perhaloalkyl;

E is selected from the group consisting of $-\text{H}$, halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, $-\text{CN}$, and $-\text{NR}^7$;

X together with Y forms a cyclic group selected from the group of heterocyclic, and aryl;

R^1 is independently selected from the group consisting of $-\text{H}$, alkyl, aryl, heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-\text{C}(\text{R}^2)_2\text{-aryl}$, $-\text{alk-aryl}$, $-\text{C}(\text{R}^2)_2\text{OC}(\text{O})\text{NR}^2$, $-\text{NR}^2\text{-C}(\text{O})\text{-R}^3$, $-\text{C}(\text{R}^2)_2\text{-OC}(\text{O})\text{R}^3$, $-\text{C}(\text{R}^2)_2\text{-O-C}(\text{O})\text{OR}^3$, $-\text{C}(\text{R}^2)_2\text{OC}(\text{O})\text{SR}^3$, $-\text{alk-S-C}(\text{O})\text{R}^3$, $-\text{alk-S-S-alkylhydroxy}$, and $-\text{alk-S-S-S-alkylhydroxy}$, or together R^1 and R^1 are $-\text{alk-S-S-alk-}$ to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together R^1 and R^1 are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-\text{R}^9$; or

together V and Z are connected via a chain of 3-5 atoms, only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy, alkoxy, or aryloxy, attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

together V and W are connected via a chain of 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy, alkoxy, alkylthiocarboxy, hydroxymethyl, or aryloxy, attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

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Q2 Z is selected from the group consisting of $-\text{CH}_2\text{OH}$, $-\text{CH}_2\text{OCOR}^3$, $-\text{CH}_2\text{OC(O)SR}^3$, $-\text{CH}_2\text{OCO}_2\text{R}^3$, $-\text{SR}^3$, $-\text{S(O)R}^3$, $-\text{CH}_2\text{N}_3$, $-\text{CH}_2\text{NR}^2_2$, $-\text{CH}_2\text{Ar}$, $-\text{CH(Ar)OH}$, $-\text{CH}(\text{CH}=\text{CR}^2_2)\text{OH}$, $-\text{CH}(\text{C}=\text{CR}^2_2)\text{OH}$, and $-\text{R}^2$;

with the provisos that:

- a) V, Z, W are not all $-\text{H}$; and
- b) when Z is $-\text{R}^2$, then at least one of V and W is not $-\text{H}$ or $-\text{R}^9$;

R^2 is selected from the group consisting of R^3 and $-\text{H}$;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

R^4 is independently selected from the group consisting of $-\text{H}$, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

R^6 is independently selected from the group consisting of $-\text{H}$, and lower alkyl;

R^7 is independently selected from the group consisting of $-\text{H}$, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and $-\text{C(O)R}^{10}$;

R^8 is independently selected from the group consisting of $-\text{H}$, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-\text{C(O)R}^{10}$, or together said R^8 groups form a bidendate alkylene;

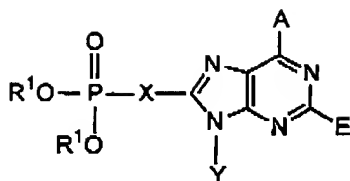
R^9 is selected from the group consisting of alkyl, aralkyl, , heteroalicyclic, and alicyclic;

R^{10} is selected from the group consisting of $-\text{H}$, lower alkyl, $-\text{NH}_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, $-\text{OH}$, $-\text{NH}_2$ and $-\text{OR}^3$; and pharmaceutically acceptable prodrugs and salts thereof.

37. (Twice Amended) A method of inhibiting gluconeogenesis in animal in need thereof, comprising administering to said animal an effective amount of a compound of formula (1):

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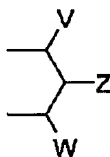
wherein

A is selected from the group consisting of $-NR^8$, $-NHSO_2R^3$, $-OR^5$, $-SR^5$, halo, lower alkyl, $-CON(R^4)_2$, guanidino, amidino, $-H$, and perhaloalkyl;

E is selected from the group consisting of $-H$, halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, $-CN$, and $-NR^7$;

X together with Y forms a cyclic group selected from the group of heterocyclic, and aryl;

R^1 is independently selected from the group consisting of $-H$, alkyl, aryl, heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)_2$ -aryl, $-alk$ -aryl, $-C(R^2)_2OC(O)NR^2$, $-NR^2-C(O)-R^3$, $-C(R^2)_2-OC(O)R^3$, $-C(R^2)_2-O-C(O)OR^3$, $-C(R^2)_2OC(O)SR^3$, $-alk-S-C(O)R^3$, $-alk-S-S-alkylhydroxy$, and $-alk-S-S-S-alkylhydroxy$, or together R^1 and R^1 are $-alk-S-S-alk-$ to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together R^1 and R^1 are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected via a chain of 3-5 atoms, only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

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Z is selected from the group consisting of $-\text{CH}_2\text{OH}$, $-\text{CH}_2\text{OCOR}^3$, $-\text{CH}_2\text{OC(O)SR}^3$, $-\text{CH}_2\text{OCO}_2\text{R}^3$, $-\text{SR}^3$, $-\text{S(O)R}^3$, $-\text{CH}_2\text{N}_3$, $-\text{CH}_2\text{NR}^2_2$, $-\text{CH}_2\text{Ar}$, $-\text{CH(Ar)OH}$, $-\text{CH}(\text{CH}=\text{CR}^2\text{R}^2)\text{OH}$, $-\text{CH}(\text{C}=\text{CR}^2)\text{OH}$, and $-\text{R}^2$;

with the provisos that:

- a) V, Z, W are not all $-\text{H}$; and
b) when Z is $-\text{R}^2$, then at least one of V and W is not $-\text{H}$ or $-\text{R}^9$;

R^2 is selected from the group consisting of R^3 and $-\text{H}$;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

R^4 is independently selected from the group consisting of $-\text{H}$, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

R^6 is independently selected from the group consisting of $-\text{H}$, and lower alkyl;

R^7 is independently selected from the group consisting of $-\text{H}$, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and $-\text{C(O)R}^{10}$;

R^8 is independently selected from the group consisting of $-\text{H}$, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-\text{C(O)R}^{10}$, or together said R^8 groups form a bidendate alkylene;

R^9 is selected from the group consisting of alkyl, aralkyl, , heteroalicyclic, and alicyclic;

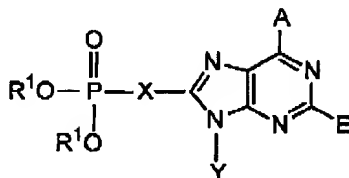
R^{10} is selected from the group consisting of $-\text{H}$, lower alkyl, $-\text{NH}_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, $-\text{OH}$, $-\text{NH}_2$ and $-\text{OR}^3$; and pharmaceutically acceptable prodrugs and salts thereof.

39. (Twice Amended) A method of treating an animal for a disease derived from abnormally elevated insulin levels, comprising administering to said animal a therapeutically

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effective amount of a fructose-1,6-bisphosphatase inhibitor wherein said inhibitor is a compound of formula (1):



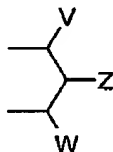
wherein

A is selected from the group consisting of $-\text{NR}^8$, $-\text{NHSO}_2\text{R}^3$, $-\text{OR}^5$, $-\text{SR}^5$, halo, lower alkyl, $-\text{CON}(\text{R}^4)_2$, guanidino, amidino, $-\text{H}$, and perhaloalkyl;

E is selected from the group consisting of $-\text{H}$, halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, $-\text{CN}$, and $-\text{NR}^7$;

X together with Y forms a cyclic group selected from the group of heterocyclic, and aryl;

R^1 is independently selected from the group consisting of $-\text{H}$, alkyl, aryl, heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-\text{C}(\text{R}^2)_2$ -aryl, $-\text{alk-aryl}$, $-\text{C}(\text{R}^2)_2\text{OC}(\text{O})\text{NR}^2$, $-\text{NR}^2-\text{C}(\text{O})-\text{R}^3$, $-\text{C}(\text{R}^2)_2-\text{OC}(\text{O})\text{R}^3$, $-\text{C}(\text{R}^2)_2-\text{O}-\text{C}(\text{O})\text{OR}^3$, $-\text{C}(\text{R}^2)_2\text{OC}(\text{O})\text{SR}^3$, $-\text{alk-S-C}(\text{O})\text{R}^3$, $-\text{alk-S-S-alkylhydroxy}$, and $-\text{alk-S-S-S-alkylhydroxy}$, or together R^1 and R^1 are $-\text{alk-S-S-alk-}$ to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together R^1 and R^1 are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-\text{R}^9$; or

together V and Z are connected via a chain of 3-5 atoms, only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy,

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hydroxymethyl, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

C-3 Z is selected from the group consisting of $-\text{CH}_2\text{OH}$, $-\text{CH}_2\text{OCOR}^3$, $-\text{CH}_2\text{OC}(\text{O})\text{SR}^3$, $-\text{CH}_2\text{OCO}_2\text{R}^3$, $-\text{SR}^3$, $-\text{S}(\text{O})\text{R}^3$, $-\text{CH}_2\text{N}_3$, $-\text{CH}_2\text{NR}^2$, $-\text{CH}_2\text{Ar}$, $-\text{CH}(\text{Ar})\text{OH}$, $-\text{CH}(\text{CH}=\text{CR}^2\text{R}^2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^2)\text{OH}$, and $-\text{R}^2$;

with the provisos that:

- a) V, Z, W are not all -H; and
- b) when Z is $-\text{R}^2$, then at least one of V and W is not -H or $-\text{R}^9$;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

R^4 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

R^6 is independently selected from the group consisting of -H, and lower alkyl;

R^7 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and $-\text{C}(\text{O})\text{R}^{10}$;

R^8 is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-\text{C}(\text{O})\text{R}^{10}$, or together said R^8 groups form a bidendate alkylene;

R^9 is selected from the group consisting of alkyl, aralkyl, , heteroalicyclic, and alicyclic;

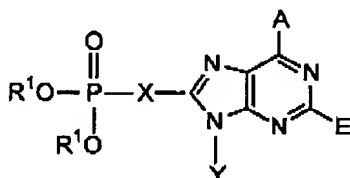
R^{10} is selected from the group consisting of -H, lower alkyl, $-\text{NH}_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, $-\text{OH}$, $-\text{NH}_2$ and $-\text{OR}^3$; and pharmaceutically acceptable prodrugs and salts thereof.

C4 42. (Twice Amended) A method of treating an animal with excess glycogen storage disease, comprising administering to said animal in need thereof a therapeutically

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effective amount of a fructose-1,6-bisphosphatase inhibitor, wherein said inhibitor is a compound of formula (1):



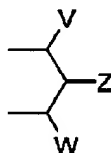
wherein

A is selected from the group consisting of $-\text{NR}^8_2$, $-\text{NHSO}_2\text{R}^3$, $-\text{OR}^5$, $-\text{SR}^5$, halo, lower alkyl, $-\text{CON}(\text{R}^4)_2$, guanidino, amidino, $-\text{H}$, and perhaloalkyl;

E is selected from the group consisting of $-\text{H}$, halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, $-\text{CN}$, and $-\text{NR}^7_2$;

X together with Y forms a cyclic group selected from the group of heterocyclic, and aryl;

R^1 is independently selected from the group consisting of $-\text{H}$, alkyl, aryl, heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-\text{C}(\text{R}^2)_2\text{-aryl}$, $-\text{alk-aryl}$, $-\text{C}(\text{R}^2)_2\text{OC}(\text{O})\text{NR}^2_2$, $-\text{NR}^2\text{-C}(\text{O})\text{-R}^3$, $-\text{C}(\text{R}^2)_2\text{-OC}(\text{O})\text{R}^3$, $-\text{C}(\text{R}^2)_2\text{-O-C}(\text{O})\text{OR}^3$, $-\text{C}(\text{R}^2)_2\text{OC}(\text{O})\text{SR}^3$, $-\text{alk-S-C}(\text{O})\text{R}^3$, $-\text{alk-S-S-alkylhydroxy}$, and $-\text{alk-S-S-S-alkylhydroxy}$, or together R^1 and R^1 are $-\text{alk-S-S-alk-}$ to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together R^1 and R^1 are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-\text{R}^9$; or

together V and Z are connected via a chain of 3-5 atoms, only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

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together V and W are connected via a chain of 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-\text{CH}_2\text{OH}$, $-\text{CH}_2\text{OCOR}^3$, $-\text{CH}_2\text{OC(O)SR}^3$, $-\text{CH}_2\text{OCO}_2\text{R}^3$, $-\text{SR}^3$, $-\text{S(O)R}^3$, $-\text{CH}_2\text{N}_3$, $-\text{CH}_2\text{NR}^2_2$, $-\text{CH}_2\text{Ar}$, $-\text{CH(Ar)OH}$, $-\text{CH}(\text{CH}=\text{CR}^2\text{R}^2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^2)\text{OH}$, and $-\text{R}^2$;

with the provisos that:

- a) V, Z, W are not all $-H$; and
- b) when Z is $-R^2$, then at least one of V and W is not $-H$ or $-R^9$;

R^2 is selected from the group consisting of R^3 and $-H$;

R³ is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl:

R^4 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

R⁶ is independently selected from the group consisting of -H, and lower alkyl;

R^7 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

R^8 is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together said R^8 groups form a bidentate alkylene;

R⁹ is selected from the group consisting of alkyl, aralkyl, , heteroalicyclic, and alicyclic;

R^{10} is selected from the group consisting of -H, lower alkyl, -NH₂, lower aryl, and lower perhaloalkyl;

R¹¹ is selected from the group consisting of alkyl, aryl, -OH, -NH₂ and -OR³; and pharmaceutically acceptable prodrugs and salts thereof.